

What is claimed is:

1. A method of inducing and/or sustaining an immunological CTL response in a mammal, which method comprises
- 5 delivering an antigen to the mammal at a level sufficient to induce an immunologic CTL response in the mammal and
- maintaining the level of the antigen in the mammal's lymphatic system over time sufficient to maintain the immunologic CTL response.
2. The method of Claim 1 wherein the CTL response is maintained by delivering the antigen directly to the animal's lymphatic system.
- 10 3. The method of Claim 2 wherein the CTL response is maintained by delivering the antigen directly to the spleen, a lymph node or lymph vessel.
4. A method of treating a mammal having a disease, or being predisposed to a disease, to which the mammal's immune system mounts a cell-mediated response to a disease-related antigen to attack the disease, which method comprises
- 15 delivering a disease-matched antigen to the animal at a level sufficient to induce an increased CTL-response in the animal and
- maintaining the increased CTL-response in the animal by sustained, regular delivery of the disease-matched antigen to the animal for a time sufficient to treat the disease wherein the sustained, regular delivery of the antigen is done in a manner that
- 20 maintains the level of antigen in the animal's lymphatic system.
5. The method of Claim 4 wherein the disease is cancer.
6. The method of Claim 5 wherein the cancer is malignant melanoma.
7. The method of Claim 4 wherein the disease is an infectious disease.
8. The method of Claim 7 wherein the infectious disease is a viral disease.
- 25 9. The method of Claim 4 wherein a single antigen is delivered to the animal.
10. The method of Claim 4 wherein multiple antigens are delivered to the animal.

11. The method of Claim 4 wherein the CTL response is maintained by delivering the antigen directly to the animal's lymphatic system.
12. The method of Claim 11 wherein the CTL response is maintained by delivering the antigen directly to a lymph node or lymph vessel.
- 5 13. The method of Claim 12 wherein the antigen is delivered directly to an inguinal or axillary lymph node.
- 10 14. The method of Claim 4 wherein the antigen is delivered to the animal by pumping a physiologically-acceptable, composition of the antigen from a device held external of the animal's body through a transmission line and catheter positioned to deliver the antigen-containing composition so that the antigen reaches the animal's lymph system.
- 15 15. The method of Claim 4 wherein the antigen is delivered by implanting an implantable, sustained-release pump containing a physiologically-acceptable, composition of the antigen at or near a site of a lymphatic organ or vessel so that the antigen-containing composition is released on a sustained regular basis over time.
16. The method of Claim 15, wherein the pump is an osmotic pump.
17. The method of Claim 4, wherein the disease is cancer and the antigen is a tumor-associated antigen.
- 20 18. The method of Claim 17, wherein the antigen is selected from the group consisting of a differentiation antigen, tumor-specific multilineage antigen, an embryonic antigen, an antigen from an expressed oncogene, an antigen from an expressed mutated tumor-suppressor gene, and a viral antigen.
- 25 19. A method according to Claim 17, wherein the antigen is selected from the group consisting of MART-1/MelanA (MART-1), gp100 (Pmel 17), tyrosinase, TRP-1, TRP-2, MAGE-1, MAGE-3, BAGE, GAGE-1, GAGE-2, p15(58), CEA p53, Ras, HER-2/neu, BCR-ABL, E2A-PRL, H4-RET, IGH-IGK, MYL-RAR, EBVA, (HPV) antigens E6 and E7, TSP-180, MAGE-4, MAGE-5, MAGE-6, RAGE, NY-ESO, p185erbB2, p180erbB-3, c-met, nm-23H1, PSA, TAG-72, CA 19-9, CA 72-4, CAM 17.1, NuMa, K-ras, H-ras, β -Catenin, CDK4, Mum-1, p15, p16.

20. A method according to Claim 4, wherein a cytokine that is capable of enhancing the CTL response is delivered and/or maintained along with the antigen.
21. A method according to Claim 20, wherein the cytokine is GM-CSF, IL-12, IL-2, TNF, IFN γ , IL-18, IL-3, IL-4, IL-8, IL-9, IL-13, IL-10, IL-14, IL-15, G-SCF, IFN alpha, IFN beta, IFN gamma, TGF alpha, TGF beta.
22. An article of manufacture for delivering an antigen that induces a CTL response in an animal, which article comprises
- a reservoir of a physiologically-acceptable, antigen-containing composition that is capable of inducing a CTL response in an animal,
- 10 a pump connected to the reservoir to deliver the composition at a defined rate,
- a transmission line to discharge the composition from the reservoir, and, optionally,
- a delivery line connected to the transmission line, which delivery line is of a size suitable for positioning in the animal and for delivery of the composition in a
- 15 manner that reaches the lymphatic system of the animal.
23. The article of Claim 22 wherein the reservoir is removable from the article of manufacture or is refillable.
24. The article of Claim 22 wherein the composition comprises only one antigen.
25. ~~The article of Claim 22 wherein the composition comprises more than one~~
- 20 antigen.
26. The article of Claim 22 wherein the composition further comprises a cytokine capable of enhancing a CTL response.
27. The article of Claim 26 wherein the cytokine is GM-CSF, IL-12, IL-2, TNF, IFN γ , IL-18, IL-3, IL-4, IL-8, IL-9, IL-13, IL-10, IL-14, IL-15, G-SCF, IFN alpha,
- 25 IFN beta, IFN gamma, TGF alpha, TGF beta.

28. The article of Claim 22 wherein the antigen is a differentiation antigen, a tumor-specific multilineage antigen, an embryonic antigen, an oncogene antigen, a mutated tumor-suppressor gene antigen, or a viral antigen.
29. The article of claim 28 wherein the antigen is selected from the group consisting of MART-1/MelanA (MART-1), gp100 (Pmel 17), tyrosinase, TRP-1, TRP-2, MAGE-1, MAGE-3, BAGE, GAGE-1, GAGE-2, p15(58), CEA, p53, Ras, HER-2/neu, BCR-ABL, E2A-PRL, H4-RET, IGH-IGK, MYL-RAR, EBVA, (HPV) antigens E6 and E7, TSP-180, MAGE-4, MAGE-5, MAGE-6, RAGE, NY-ESO, p185erbB2, p180erbB-3, c-met, nm-23H1, PSA, TAG-72, CA 19-9, CA 72-4, CAM 17.1, NuMa, K-ras, H-ras, β -Catenin, CDK4, Mum-1, p15, p16.
30. The article of Claim 22 wherein the article is an external device and the delivering line is a catheter that is long enough for delivery to the animal subcutaneously or lymphatically.
31. The article of Claim 30 wherein the catheter is long enough for delivery directly to the lymphatic system of the animal.
32. The article of Claim 31 wherein the delivery to the lymphatic system is through an axillary or inguinal node.
33. The article of Claim 22 that is portable.
34. The article of Claim 33 that is of a size suitable for portably attaching to a human.
35. The article of Claim 22 wherein the pump is a roller/peristaltic pump, a syringe pump, a piston/valve pump, or a gas pressure pump.
36. The article of Claim 22 wherein the pump is battery operated.
37. The article of Claim 22 in combination with printed instructions for delivery of the antigen composition on a regular basis over time to maintain the antigen in the animal's lymphatic system at a level sufficient to maintain a CTL response in the animal.

38. A process for preparing a system useful for inducing a sustained CTL response in an animal needing such a response, which comprises:

placing a physiologically-acceptable, aqueous, antigen-containing composition in a reservoir having a pump for delivering the composition at a defined rate through a transmission line to the animal.